REMARKS/ARGUMENTS

Claims 1-14, 16, 19-44, 46-48, 50-60, 64, and 65 were pending in the present application before this Preliminary Amendment as set forth above. By the Preliminary Amendment, claims 1, 27, 28, 31, 33, and 60 are amended and claims 25 and 26 are canceled without prejudice.

In the Final Office Action mailed October 25, 2010 (hereinafter "the Office Action"), claims 1-5, 8-14, 16, 19-38, 41-44, 46-48, 50-60, 64, and 65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Publication No. 2003/0003571 to Kanegasaki et al. (hereinafter "Kanegasaki"), in view of U.S. Patent No. 5,520,787 to Hanagan et al. (hereinafter "Hanagan") and U.S. Patent No. 5,589,352 to Breznak et al. (hereinafter "Breznak").

Applicant very much appreciates the Primary Examiner's careful review of the instant application, and for granting and conducting a telephone interview on January 21, 2011 with Dr. Tim Tingkang Xia and Christopher W. Glass, both Patent Attorneys for Applicant on the record. During the telephone interview, the Office Action was discussed, as well as proposed amendments to independent claims 1, 33, and 60. For example, Applicant proposed amending claim 1 to recite a fourth substrate having optical measurement means, and amending each of claims 33 and 60 to recite an optical measurement means, where the electrochemical measurement means is positioned between and in communication with the substrate and optical measurement means. The Primary Examiner suggested that Applicant amend the claims to include the proposed amendments in a Response to the Office Action.

In response, as set forth above, claims 1, 33, 60, 27, 28, 31, 33, and 60 are amended for better form and according to the Primary Examiner's suggestions. For example, claim 1 is amended to incorporate features recited in original claims 25 and 26, now canceled. Also, each of claims 33 and 60 are amended to recite features directed to optical measurement means, as set forth in the disclosure as originally filed. Without acquiescing in the propriety of the Primary Examiner's rejections and to facilitate the prosecution of the present application, as set forth above, claims 25 and 26 are canceled. Applicant reserves every right in canceled claims 25 and 26 to file continuation applications.

Support for the amendments can be found in the disclosure as originally filed, for example in the original claims, in paragraphs on page 20, lines 25-37 to page 27, lines 1-34 of the specification, and in Figs. 1A, 1B, and 2 of the drawings. Applicant submits that no new

matter is added.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is now believed that the application is in condition for allowance at least for the reasons set forth below and such allowance is respectfully requested.

The following remarks herein are considered to be responsive thereto.

Rejections under 35 U.S.C. § 103

In the Office Action, claims 1-5, 8-14, 16, 19-38, 41-44, 46-48, 50-60, 64, and 65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak. Applicant respectfully traverses the rejections for at least the reasons set forth below.

Claims 1-14, 16, 19-24, and 27-32:

As set forth above, amended claim 1 recites "[a] bioreactor for cultivating living cells in a liquid medium comprising:

(a) a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium;

(b) a barrier dividing the chamber into a first subchamber and a second subchamber, wherein the barrier comprises a porous material and has a porosity to allow the first subchamber and the second subchamber to be in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber and the second subchamber;

(c) a second substrate positioned adjacent to the first surface of the first substrate;

(d) a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate;

(e) ***an electrochemical measuring system positioned in the third substrate*** and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber;

(f) ***a fourth substrate positioned above the third substrate such that the third substrate forms an intermediate layer between the first substrate and the fourth substrate; and***

(g) ***means positioned in the fourth substrate and adapted for optical measurements of the cells*** responsive to the liquid medium in at least one of the first subchamber and the second subchamber." (Emphasis added.)

As described in paragraphs on page 20, lines 24-38 through page 24, lines 1-20 of the specification as originally filed and as shown in Figs. 1A and 1B of the drawings as originally filed, in one embodiment of the present invention a bioreactor 100 has a first substrate 140 having a first surface 140a and an opposite second surface 104b, defining a chamber 101 therebetween for receiving cells and a liquid medium. The bioreactor 100 has a barrier 104 dividing the chamber 101 into a first subchamber 102 and a second subchamber 103, wherein the barrier 104 has a porosity to allow the first subchamber 102 and the second subchamber 103 in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber 102 and the second subchamber 103. Moreover, the bioreactor 100 has a second substrate 150, wherein the second substrate 150 is positioned adjacent to the first surface 140a of the first substrate 140 and defines a plurality of connection channels 155. The bioreactor 100 further has ***a third substrate 160, which is positioned adjacent to the first surface of the first substrate 140, and means 161-165 strategically positioned in the third substrate 160 and adapted for electrochemical measurements of the cells*** responsive to the liquid medium in one or both of the first subchamber 102 and the second subchamber 103. In one embodiment as shown in Fig. 1B, the means for electrochemical measurements includes a reference electrode 161, a counter electrode 162, a plurality of edge connector pads 164, a plurality of electrically conductive leads 163, and a plurality of individually addressable working electrodes 165. Further, ***a fourth substrate 170 is positioned above the second surface 140b of the first substrate 140, with means 171-174 strategically positioned in the fourth substrate 170 for***

optical measurements of the cells responsive to the liquid medium in at least one of the first subchamber 102 and the second subchamber 103. In the embodiment as shown in Fig. 1B, the means for optical measurements includes a plurality of optical sensors 171, and ***the means for electrochemical measurements 161-165 is positioned between the means 171-174 for optical measurements in the fourth substrate 170, and the first substrate 140***.

As understood by Applicant, Kanegasaki discloses "a well unit to be used in an apparatus whereby movements of cells based on their own actions" can be detected. (Kanegasaki, [0009].) In one embodiment as shown in Fig. 6 of Kanegasaki, a well unit including a substrate 7 and an optically transparent glass substrate 8 has a channel 1 and wells 2A and 2B in which a sample such as a cell suspension or a specimen solution is contained. In operation, a sample is supplied into the well 2A or 2B through a tube 3A or 3B, and after cell migration, cells are collected from the well 2A or 2B through the tube 3A or 3B (see e.g. Kanegasaki, [0087]-[0088].) As shown in Fig. 6 of Kanegasaki, a microscope 13 externally disposed in relation to the well unit is used for optical detection. Kanegasaki further discloses that "[f]or detection in integrated [well] units, it is preferable to employ a system wherein the channels of the units are successively scanned along with an objective lens." (Kanegasaki, [0163].)

In the Office Action, the Examiner concedes on page 4 that Kanegasaki does not disclose that the third substrate includes a means for electrochemical measurement. In other words, ***Kanegasaki does not disclose "means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber,"*** as recited in amended claim 1. (Emphasis added.)

Further, Applicant submits that Kanegasaki does not disclose, teach, or suggest "***a fourth substrate positioned above the third substrate such that the third substrate forms an intermediate layer between the first substrate and the fourth substrate; and means positioned in the fourth substrate and adapted for optical measurements of the cells*** responsive to the liquid medium in at least one of the first subchamber and the second subchamber," as recited in amended claim 1.

The Examiner attempts to cure the deficiencies of Kanegasaki using the disclosures of Hanagan and Breznak. Hanagan, as understood by Applicant, discloses "a diagnostic flow cell for determining the presence or amount of an analyte which may be contained in a test sample." (Hanagan, Abstract.) Hanagan shows in Fig. 1 a flow channel defined by "longitudinal voids 66 and 56" with electrodes comprising conductive traces 30 that are disposed linearly along the flow channel and positioned above and covering the flow channel. (Hanagan, Col. 8, lines 1-28.) Breznak, as understood by Applicant, discloses a system and method for "observation of microorganisms in a controlled environment" using a diffusion gradient chamber with reservoirs. (Breznak, Abstract.)

Applicant respectfully submits that neither Hanagan nor Breznak, taken alone or in combination, disclose, teach, or suggest a bioreactor having "***means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber" and "a fourth substrate positioned above the third substrate such that the third substrate forms an intermediate layer between the first substrate and the fourth substrate; and means positioned in the fourth substrate and adapted for optical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber,***" as recited in amended claim 1.

Therefore, none of Hanagan and/or Breznak cure the deficiencies of Kanegaski, and accordingly, none of Kanegasaki, Hanagan, and/or Breznak disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1.

For at least the reasons set forth above, Applicant respectfully submits that the Examiner has failed to make a *prima facie* case to support the rejection of amended claim 1 under 35 U.S.C. §103(a) over Kanegasaki, Hanagan, and/or Breznak. First, there is no suggestion or motivation to modify the references or combine the reference teachings. Second, there is no reasonable expectation of success of combining the reference teachings. Finally, the combination of references does not teach or suggest all elements of Applicant's claims.

In supporting the obviousness rejections under 35 U.S.C. §103, the Examiner "bears ***the initial burden…of presenting a prima facie case of unpatentability***…After evidence or argument is submitted by the applicant in response, patentability is determined ***on the totality of***

the record." *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733 (January 14, 2008), and "***Office personnel must articulate***", among other things, "***a finding that the prior art included each element claimed*** ...", MPEP 2143 (A)(1). The "***unwitting application of hindsight" is inappropriate***. *Ex parte So and Thomas*, BPAI Appeal No. 2007-3967 (January 4, 2008). In other words, the Examiner's "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). (MPEP § 2142). (Emphasis added.)

For at least the foregoing reasons, Applicant respectfully submits that claim 1, as amended, is patentable under 35 U.S.C. §103(a) over any combination of Kanegasaki, Hanagan, and/or Breznak.

Accordingly, claims 14, 16, 19-24, and 27-32, which depend from now allowable amended claim 1, are also patentable for at least this reason.

Claims 33-44, 46-48, and 50-59:

As set forth above, amended claim 33 recites "[a] bioreactor for cultivating living cells in a liquid medium comprising:

(a) ***a substrate*** having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium, wherein the chamber is formed with a center and a boundary;

(b) a first barrier enclosing the center and a portion of the chamber to form a central chamber;

(c) a second barrier positioned between the first barrier and the boundary so as to form an intermediate chamber and an outer chamber;

(d) ***means for electrochemical measurements of the cells*** responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber; and

(e) ***means for optical measurements of the cells*** responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber, and the central chamber,

wherein the means for electrochemical measurements ***is positioned between and in communication with the substrate and the means for optical measurements***,

wherein the first barrier has a first porosity to allow the central chamber and the intermediate chamber to be in fluid communication and allow at least a first predetermined type of cells to permeate between the central chamber and the intermediate chamber, the second barrier has a second porosity to allow the outer chamber and the intermediate chamber to be in fluid communication and allow at least a second predetermined type of cells to permeate between the outer chamber and the intermediate chamber, and wherein the first barrier comprises a porous material." (Emphasis added.)

As described in paragraphs on page 24, lines 23-38 to page 27, lines 1-34 of the specification as originally filed and as shown in Fig. 2 of the drawings as originally filed, in one embodiment of the present invention, a bioreactor 700 includes a substrate 730 having a first surface and an opposite second surface, defining a chamber 732 therebetween for receiving cells and a liquid medium, where the chamber 732 is formed with a center 734 and a boundary 736. A first barrier 738 encloses the center 734 and a portion of the chamber 732 to form a central chamber 706, and a second barrier 740, which is positioned between the first barrier 738 and the boundary 736 so as to form an intermediate chamber 705 and an outer chamber 704.

Applicant respectfully submits that none of Kanegasaki, Hanagan, and/or Breznak, taken alone or in combination, disclose a bioreactor having "***a substrate*** having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells and receiving the liquid medium, wherein the chamber is formed with a center and a boundary; a first barrier enclosing the center and a portion of the chamber to form a central chamber; a second barrier positioned between the first barrier and the boundary so as to form an intermediate chamber and an outer chamber; ***means for electrochemical measurements of the cells*** responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber; and ***means for optical measurements of the cells*** responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber, and the central chamber, ***wherein the means for electrochemical measurements is positioned between and in communication with the substrate and the means for optical measurements,***" as recited in amended claim 33. (Emphasis added.)

For at least these reasons and also incorporating herewith the reasons set forth above why amended claim 1 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak, Applicant respectfully submits that amended claim 33 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak.

Accordingly, claims 34-44, 46-48, and 50-59, which depend from now allowable amended claim 33, are also patentable for at least this reason.

Claims 60, 64, and 65:

As set forth above, claim 60 recites "[a] bioreactor for cultivating living cells in a liquid medium comprising:

(a) a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving and culturing the cells, and receiving the liquid medium with a boundary; and

(b) means for dividing the chamber into plurality of chambers;

(c) ***means for electrochemical measurements of the cells*** responsive to the liquid medium in at least one of the plurality of chambers; and

(d) ***means for optical measurements of the cells*** responsive to the liquid medium in at least one of the plurality of chambers,

wherein the means for electrochemical measurements is positioned between and in communication with the substrate and the means for optical measurements,

wherein each of the plurality of subchambers is in fluid communication with at least another one of the plurality of subchambers, wherein the dividing means comprises a barrier to divide the chamber into a first subchamber and a second subchamber, wherein the barrier has a porosity to allow the first subchamber and the second subchamber to be in fluid communication and to allow at least one predetermined type of cells to permeate between the first subchamber and the second subchamber, and wherein the barrier comprises a porous material." (Emphasis added.)

Incorporating herewith the reasons set forth above why amended claims 1 and 33 are patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak, Applicant

respectfully submits that amended claim 60 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak for at least these reasons.

Accordingly, claims 64 and 65, which depend from now allowable amended claim 60, are also patentable for at least this reason.

CONCLUSION

Applicant respectfully submits that the foregoing Preliminary Amendment places this application in condition for allowance. If the Primary Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, to facilitate the prosecution, please call the undersigned at 404.495.3678. The Commissioner is hereby authorized to charge any petition fee under 37 CFR 1.17(f),(g) or (h) or any deficiency of fees and credit of any overpayments to Deposit Account No. 50-3537.

Respectfully submitted,

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